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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/674,836	09/29/2003	Gregg B. Morin	082/103C	5541

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EXAMINER	
ANGELL, JON E	
ART UNIT	PAPER NUMBER
1635	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/18/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/674,836	MORIN ET AL	
	Examiner	Art Unit	
	Jon Eric Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 January 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11,13-16 and 18-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,13-16 and 18-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/31/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Action is in response to the communication filed on 1/31/2007.

The amendment filed 1/31/2007 is acknowledged and has been entered.

Applicant's arguments are addressed on a per section basis. The text of those sections of Title 35, U.S. Code not included in this Action can be found in a prior Office Action. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims and/or applicant's arguments.

Claims 1-11, 13-16, 18-32 are currently pending in the application and are addressed herein.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 1/31/2007 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Duplicate Claims Warning

Applicant is advised that should claim 25 be found allowable, claim 26 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Here, claims 25 and 26 are substantially identical.

Claim Rejections - 35 USC § 112, first paragraph-Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2, 3, 18, 19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

Claims 2, 3, 18, 19 encompass a sequence which comprises the promoter contained in the APAI-FSPI fragment just upstream of the encoding sequence of hTERT or a sequence which hybridizes to DNA complementary to said APAI-FSPI fragment, wherein the promoter sequence causes a transcribable to be expressed in cells that endogenously express TERT. As such, these claims encompass any promoter sequence or fragment/variant thereof that is comprised in the indicated fragment including promoter sequences, wherein the sequence causes a transcribable to be expressed in cells that endogenously express TERT. Looking to the specification for guidance, the specification has only disclosed a fragment comprising nucleotides –117 to –39

and a fragment comprising nucleotides from –239 to –36 from the translation initiation site of SEQ ID NO:1 as the particular sequences which have the indicated function. Therefore, based on the specification as disclosed, and in view of the prosecution history of the parent application which has been allowed as Patent No. 6,777,203, the specification has only provided sufficient description of promoter sequences which comprise sequences which are at least 80% identical to sequences –117 to –39 and sequences –239 to –36 the from the translation initiation site of SEQ ID NO:1 and which cause the encoded region to be transcribed in human cells which express hTERT. There is no disclosure in the specification which would allow one of skill in the art to determine which sequences encompassed by the claims (other than the sequences comprising –239 to –36 or –117 to –36) actually cause a transcribable to be expressed in cells that endogenously express TERT and which ones don't, without performing additional experimentation.

Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). Here, the skilled artisan cannot envision the detailed chemical structure of the molecules encompassed by the claimed genus (other than the specifically indicate sequences),

and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

Claim Rejections - 35 USC § 112, first paragraph-Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-11, 13-16 and 21-32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

(1) A method of expressing a transcribable nucleotide sequence in a mammalian cell that expresses TERT, comprising directly administering to said cell a polynucleotide sequence comprising a promoter operably linked to a heterologous encoding sequence wherein the promoter comprises nucleotides sequences which are at least 80% identical to nucleotides –117 to –39 or –239 to –36 from the translation initiation site of SEQ ID NO:1 and which causes the encoding sequence to be transcribed in said cells; and,

(2) A method of killing a mammalian cell that expresses TERT or a method of treating cancer, comprising directly administering to the target cell a polynucleotide sequence comprising a promoter operably linked to an encoding sequence which encodes a substance which is toxic to the cell, wherein the promoter comprises nucleotides sequences which are at least 80% identical to nucleotides –117 to –39 or –239 to –36 from the translation initiation site of SEQ ID NO:1 and which causes the encoding sequence to be transcribed in said cells, thereby killing the said cells;

does not reasonably provide enablement for the full scope encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is

most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988).

> *Wands* states on page 1404,
> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The invention is in a class of invention which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." Mycogen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Fed. Cir. 2001).

The issues with the instant claims are (1) the promoter sequence must comprises a sequence that is at least 80% identical to nucleotides –117 to –39 or –239 to –36 from the translation initiation site of SEQ ID NO:1, and (2) that the polynucleotide sequence must be administered directly to cell.

With respect to the promoter sequences encompassed by the claims, as indicated above, the claims encompass a sequence which comprises the promoter contained in the APAI-FSPI fragment just upstream of the encoding sequence of hTERT or a sequence which hybridizes to DNA complementary to said APAI-FSPI fragment, wherein the promoter sequence causes a transcribable to be expressed in cells that endogenously express TERT. Considering the vast possible number of different sequences which could be encompassed by the claims, it would take

an enormous amount of additional experimentation in order to determine which sequences were functional and which ones were not.

Furthermore, all of the claims encompass embodiments where the encoded sequence is expressed in a cell that is in vivo. Given the broadest reasonable interpretation of the claims consistent with the specification, the claims encompass administering the polynucleotide which expresses the encoded sequence by any route of administration, including general systemic administration. However, the relevant art teaches that there are a number of obstacles for delivering a polynucleotide of interest to a specific target cell by systemically administering the polynucleotide.

For instance, regarding gene therapy in general, Anderson (Nature 1998; 392(suppl):25-30) teaches,

> The challenge is to develop gene therapy as an efficient and safe drug delivery system. The goal is more difficult to achieve than many investigators had predicted... The human body has spent many thousands of years learning to protect itself from the onslaught of environmental hazards, including the incorporation of foreign DNA into its genome. (See p. 25, second paragraph). The ultimate goal of gene therapy research is the development of vectors that can be injected, will target specific cells, will result in safe and efficient gene transfer into a high percentage of those cells, will insert themselves into appropriate regions of the genome (or will persist as stable episomes), will be regulated be either by administered agents or by the body's own physiological signals, will be cost effective and will cure disease. (See p. 30, first paragraph).

Crystal (Science 1995; 270:404-410) also indicates some of the problems regarding gene therapy in general. Specifically, regarding the obstacles of human gene transfer, Crystal teaches, "The [gene transfer] vector (should) be specific for its target, not recognized by the immune system..." (See p. 409, column 2 under "The perfect vector").

Finally, regarding the delivery of gene therapy vectors to tumors, but applicable to the specific delivery of all gene therapy molecules, Greco (Frontiers in Biosci. 2002; 7:d1516-1524) teaches,

> The administration of gene therapy vectors requires that they be not only targeted, but also protected from degradation, sequestration or immune attack, in order to reach the appropriate sites for transfection. Although some success has been reported for naked DNA, efficient delivery has been restricted to intratumoral injection. (see p. 1517, paragraph bridging columns 1-2).

Indicating that direct delivery of the nucleic acid to the desired site of transfection is critical for delivering the nucleic acid to the appropriate cells.

It is noted that the specification does not provide the necessary guidance to overcome the problems recognized in the art with respect to systemic delivery of a polynucleotide sequence.

Therefore, additional experimentation would be required. The additional is not considered routine and would amount to significant advancement above the state of the art at the time of filing. As such, the additional experimentation is considered undue.

Considering the nature of the invention, the breadth of the claims, the unpredictable nature of the invention as recognized in the prior art, the limited amount of working examples and guidance provided, and the high degree of skill required to practice the invention, it is concluded that the specification does not provide an enabling disclosure for the full scope encompassed by the instant claims. Therefore, additional experimentation is required before one of skill in the art could make and use the claimed invention. The amount of additional experimentation required to perform the broadly claimed invention is undue.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-11, 13-16, 21-32 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-19, 22 and 23 of U.S. Patent No. 6,777,203. Although the conflicting claims are not identical in scope, they are not patentably distinct from each other because the claims are drawn to the same subject matter, but the instant claims are broader in scope than the claims in Patent 6,777,203. Therefore, the patented claims are a species of the instant claimed genus. Since a species claim anticipates a genus claims, the instant claims are anticipated by the claims of the '203 patent.

Response to Arguments

Applicant's arguments filed 10/17/2006 have been fully considered.

With respect to the rejection of claims 2, 3, 18 and 19 under 35 U.S.C. 112, first paragraph (written description), Applicants argue that the claims have been amended to state more explicitly that the promoter used in the polynucleotide (either the prototype hTERT sequence or a variant) causes the transcribable sequence to be expressed in cells endogenously expressing TERT.

In response, it is acknowledged that the instant claims now indicate that the promoter used in the polynucleotide (either the prototype hTERT sequence or a variant) causes the transcribable sequence to be expressed in cells endogenously expressing TERT. However, the instant claims still encompass a sequence which comprises the promoter contained in the APAI-FSPI fragment just upstream of the encoding sequence of hTERT or a sequence which hybridizes to DNA complementary to said APAI-FSPI fragment, wherein the promoter sequence causes a transcribable to be expressed in cells that endogenously express TERT. As such, these claims encompass any promoter sequence or fragment/variant thereof that can hybridize to the indicates sequence in the indicated condition and, wherein the sequence causes a transcribable to be expressed in cells that endogenously express TERT. Since the specification does not provide and adequate description for the claimed genus of molecules, applicants arguments are not persuasive.

With respect to the rejection of claims under 35 U.S.C. 112, first paragraph (scope of enablement), Applicants argue that there is quite a large literature validating the use of gene therapy vectors for cancer treatment, and cites 5 specific references.

In response, all of the cited references have been fully considered by the Examiner. It is respectfully pointed out that the rejection is based on 2 main issues: (1) the promoter sequence must comprises a sequence that is at least 80% identical to nucleotides –117 to –39 or –239 to –36 from the translation initiation site of SEQ ID NO:1, and (2) that the polynucleotide sequence must be administered directly to cell.

Applicants have not presented a rebuttal to issue (1). Furthermore, it is respectfully pointed out that the claims must be enabled at the time of filing, which is considered to be at least as early as 2/4/1999. However, all of the cited references were published well after the time the invention was filed. Therefore, the cited references do not demonstrate the claimed invention was enabled at the time of filing.

Therefore, Applicants arguments are not persuasive.

With respect to the Obvious-type Double patenting rejection, no terminal disclaimer has been filed and applicants have presented a rebuttal to the rejection. As such, the rejection stands for the reasons indicated herein.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon Eric Angell whose telephone number is 571-272-0756. The examiner can normally be reached on 9:00 a.m.- 5:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Douglas Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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